Medullary thyroid cancer

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Medullary thyroid cancer is a form of thyroid carcinoma which originates from the *parafollicular cells* (C cells), which produce the hormone calcitonin.

Approximately 25% the cancer develops in families. When MTC occurs by itself it is termed familial MTC; when it coexists with tumors of the parathyroid gland and medullary component of the adrenal glands (pheochromocytoma) it is called multiple endocrine neoplasia type 2 (MEN2).

It was first characterized in 1959.[1]

Medullary thyroid cancer *Classification and external resources*	
ICD-10	C73. (http://www.who.int/classifications/apps/icd/icd10online/?gc73.htm+c73)
ICD-9	193 (http://www.icd9data.com/getICD9Code.ashx?icd9=193)
OMIM	155240 (http://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=155240)
eMedicine	med/2272 (http://www.emedicine.com/med/topic2272.htm)
MeSH	D013964 (http://www.nlm.nih.gov/cgi/mesh/2009/MB_cgi?field=uid&term=D013964)

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Markers

While the increased serum concentration of calcitonin is not harmful, it is useful as a marker which can be tested in blood. [2]

A second marker, carcinoembryonic antigen (CEA), also produced by medullary thyroid carcinoma, is released into the blood and it is useful as a serum or blood tumor marker. In general measurement of serum CEA is less sensitive than serum calcitonin for detecting the presence of a tumor, but has less minute to minute variability and is therefore useful as an indicator of tumor mass.

Genetics

Mutations (DNA changes) in the RET proto-oncogene, located on chromosome 10, lead to the expression of a mutated receptor tyrosine kinase protein, termed RET. RET is involved in the regulation of cell growth and development and its mutation is responsible for nearly all cases of hereditary or familial medullary thyroid carcinoma. Its mutation may also be responsible for the development of hyperparathyroidism and pheochromocytoma. Hereditary medullary thyroid cancer is inherited as an

autosomal dominant trait, meaning that each child of an affected parent has a 50/50 probability of inheriting the mutant RET proto-oncogene from the affected parent. DNA analysis makes it possible to identify children who carry the mutant gene; surgical removal of the thyroid in children who carry the mutant gene is curative if the entire thyroid gland is removed at an early age, before there is spread of the tumor. The parathyroid tumors and pheochromocytomas are removed when they cause clinical symptomatology. Hereditary medullary thyroid carcinoma or multiple endocrine neoplasia (MEN2) accounts for approximately 25% of all medullary thyroid carcinomas.

Seventy-five percent of medullary thyroid carcinoma occurs in individuals without an identifiable family history and is assigned the term "sporadic". Individuals who develop sporadic medullary thyroid carcinoma tend to be older and have more extensive disease at the time of initial presentation than those with a family history (screening is likely to be initiated at an early age in the hereditary form). Approximately 25-60% of sporadic medullary thyroid carcinomas have a somatic mutation (one that occurs within a single "parafollicular" cell) of the RET proto-oncogene. This mutation is presumed to be the initiating event, although there could be other as yet unidentified causes.

Clinical features

The major clinical symptom of metastatic medullary thyroid carcinoma is diarrhea; occasionally a patient will have flushing episodes. Both occur particularly with liver metastasis. Occasionally, diarrhea or flushing will be the initial presenting complaint. The flushing that occurs in medullary thyroid carcinoma is indistinguishable from that associated with carcinoid syndrome. The presumed cause of flushing and diarrhea is the excessive production of calcitonin gene products (calcitonin or calcitonin gene-related peptide) and differs from the causation of flushing and diarrhea in carcinoid syndrome. Sites of spread of medullary thyroid carcinoma include local lymph nodes in the neck, lymph nodes in the central portion of the chest (mediastinum), liver, lung, and bone. Spread to other sites such as skin or brain occurs but is uncommon.